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             181  PROHIBITIN
      S1       0  P66 AND PROHIBITIN
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              11  AU=MADIREDDI MALAVI T
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0014388500   BIOSIS NO.: 200300347219
Effect of testosterone and castration on whole body oxygen consumption,
  heart size and skeletal muscle size in lean rats.
AUTHOR: Beehler Blake (Reprint); Sleph Paul G; Egan Donald; Welzel Gustav;
  Cheng Lin; Lupisella John; Ostrowski Jacek; %%%Madireddi Malavi%%%;
  Grover Gary J
AUTHOR ADDRESS: Metabolic and Cardiovascular Drug Discovery, Bristol-Myers
  Squibb Company, 311 Pennington-Rocky Hill Road, Pennington, NJ, 08534,
  USA**USA
AUTHOR E-MAIL ADDRESS: blake.beehler@bms.com; paul.sleph@bms.com;
  donald.egan@bms.com; gustav.welzel@bms.com; lin.cheng@bms.com;
  john.lupisella@bms.com; jacek.ostrowski@bms.com; malavi.madireddi@bms.com
  ; gary.grover@bms.com
JOURNAL: FASEB Journal  17 (4-5): pAbstract No. 320.18 March 2003 2003
MEDIUM: e-file
CONFERENCE/MEETING: FASEB Meeting on Experimental Biology: Translating the
Genome  San Diego, CA, USA  April 11-15, 2003; 20030411
SPONSOR: FASEB
ISSN: 0892-6638 _(ISSN print)
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Testosterone (T) has no effect on skeletal muscle growth in rats
  except levator ani (LA) muscle, but T may affect whole body oxygen
  consumption (MVO2). Our goal was to show the effect of T on MVO2 and
  compare this to heart and skeletal muscle size and molecular markers.
  Rats were surgically castrated and 2 wks later were treated with 0.001-3
  mg/kg/day T (s.c.) for 2 and 8 wks. Castration caused marked atrophy of
  LA at 2 and 8 wks and T rescued them (ED50 = 0.08 mg/kg/day, 8 wks). No
  effects on plantaris (P) or extensor digitorum longus (EDL) muscles were
  seen for any treatment while T increased heart weight (14+-1%, 3
  mg/kg/day, 8 wks). Myostatin (mst) mRNA levels increased 2-3 fold at 72 h
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of castration in LA, P and EDL while kallikrein-7 (klk7) mRNA levels decreased. T reduced LA mst mRNA within 48 hrs while P and EDL levels were reduced by 144 h. T increased klk7 mRNA as early as 48 h in LA, P and EDL. No changes were observed in cardiac mst. Castration reduced Klk1 in heart by 72 h and increased it by 48 h of T. MVO2 was significantly reduced in castrated rats and was unaffected at 2 wks of T, but at 8 wks, dose-dependent increases were seen (17+-4% at 3 mg/kg). Adiposity in T treated animals was reduced in parallel with MVO2 changes. Therefore, mst and klk7 may serve as early indicators of T activity in muscle which may be distinct from muscle growth, while MVO2 is a reliable and dose-dependent index of T activity in rats. This may have implications for the clinic.

2/7/2
DIALOG(R)File 5:Biosis Previews(R)

0013564516 BIOSIS NO.: 200200158027
Lack of molecular evidence for motilin receptor (GPR-38) subtypes in GI tract and CNS
AUTHOR: Yan Mujing (Reprint); %%%Madireddi Malavi%%%; Gray Kevin; Sasseville Vito; Gordon David
AUTHOR ADDRESS: Hopewell Biology, Bristol-Myers Squibb Co., 311 Pennington-Rocky Hill Rd., Pennington, NJ, 08502, USA**USA
JOURNAL: Molecular Biology of the Cell 12 (Supplement): p360a Nov, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 41st Annual Meeting of the American Society for Cell Biology Washington DC, USA December 08-12, 2001; 20011208
SPONSOR: American Society for Cell Biology
ISSN: 1059-1524
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/3
DIALOG(R)File 5:Biosis Previews(R)

0013385562 BIOSIS NO.: 200100557401
Genomic structure, chromosomal localization and expression profile of a novel melanoma differentiation associated (mda-7) gene with cancer specific growth suppressing and apoptosis inducing properties
AUTHOR: Huang Eric Y; %%%Madireddi Malavi T%%%; Gopalkrishnan Rahul V; Leszczyniecka Magdalena; Su Zao-zhong; Lebedeva Irina V; Kang Dong-chul; Jiang Hongping; Lin Jiao Jiao; Alexandre Deborah; Chen Yinming; Vozhilla Nicollaq; Mei Mei Xin; Christiansen Keith A; Sivo Frank; Goldstein Neil I ; Mhashilkar Abner B; Chada Sunil; Huberman Eliezer; Pestka Sidney; Fisher Paul B (Reprint
AUTHOR ADDRESS: Departments of Pathology and Urology, College of Physicians and Surgeons, Columbia University, 630 West 168th Street, New York, NY, 10032, USA**USA
JOURNAL: Oncogene 20 (48): p7051-7063 25 October, 2001 2001
MEDIUM: print
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Abnormalities in cellular differentiation are frequent occurrences in human cancers. Treatment of human melanoma cells with recombinant fibroblast interferon (IFN-beta) and the protein kinase C activator mezerein (MEZ) results in an irreversible loss in growth potential, suppression of tumorigenic properties and induction of terminal cell differentiation. Subtraction hybridization identified melanoma differentiation associated gene-7 (mda-7), as a gene induced during these physiological changes in human melanoma cells. Ectopic expression of mda-7 by means of a replication defective adenovirus results in growth suppression and induction of apoptosis in a broad

spectrum of additional cancers, including melanoma, glioblastoma multiforme, osteosarcoma and carcinomas of the breast, cervix, colon, lung, nasopharynx and prostate. In contrast, no apparent harmful effects occur when mda-7 is expressed in normal epithelial or fibroblast cells. Human clones of mda-7 were isolated and its organization resolved in terms of intron/exon structure and chromosomal localization. Hu-mda-7 encompasses seven exons and six introns and encodes a protein with a predicted size of 23.8 kDa, consisting of 206 amino acids. Hu-mda-7 mRNA is stably expressed in the thymus, spleen and peripheral blood leukocytes. De novo mda-7 mRNA expression is also detected in human melanocytes and expression is inducible in cells of melanocyte/melanoma lineage and in certain normal and cancer cell types following treatment with a combination of IFN-beta plus MEZ. Mda-7 expression is also induced during megakaryocyte differentiation induced in human hematopoietic cells by treatment with TPA (12-O-tetradecanoyl phorbol-13-acetate). In contrast, de novo expression of mda-7 is not detected nor is it inducible by IFN-beta + MEZ in a spectrum of additional normal and cancer cells. No correlation was observed between induction of mda-7 mRNA expression and growth suppression following treatment with IFN-beta + MEZ and induction of endogenous mda-7 mRNA by combination treatment did not result in significant intracellular MDA-7 protein. Radiation hybrid mapping assigned the mda-7 gene to human chromosome 1q, at 1q 32.2 to 1q41, an area containing a cluster of genes associated with the IL-10 family of cytokines. Mda-7 represents a differentiation, growth and apoptosis associated gene with potential utility for the gene-based therapy of diverse human cancers.

2/7/4
DIALOG(R)File 5:Biosis Previews(R)

0012700698 BIOSIS NO.: 200000419011
AP-1 and C/EBP transcription factors contribute to mda-7 gene promoter activity during human melanoma differentiation
AUTHOR: %%%Madireddi Malavi T%%%; Dent Paul; Fisher Paul B (Reprint
AUTHOR ADDRESS: College of Physicians and Surgeons, Departments of Pathology and Urology, Columbia University, 630 West 168th Street, BB-1501, New York, NY, 10032, USA**USA
JOURNAL: Journal of Cellular Physiology 185 (1): p36-46 October, 2000 2000
MEDIUM: print
ISSN: 0021-9541
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Treatment of human melanoma cells with a combination of recombinant fibroblast interferon (IFN-beta) and the protein kinase C (PKC) activator mezerein (MEZ) causes a rapid and irreversible suppression in growth and terminal cell differentiation. Temporal subtraction hybridization combined with random clone selection, reverse Northern hybridization, high throughput microchip cDNA array screening, and serial cDNA library arrays permit the identification and cloning of genes that are differentially expressed during proliferative arrest and terminal differentiation in human melanoma cells. A specific melanoma differentiation associated (mda) gene, mda-7, exhibits reduced expression as a function of melanoma progression from melanocyte to metastatic melanoma. In contrast, treatment of metastatic melanoma cells with IFN-beta + MEZ results in expression of mda-7 mRNA and protein. To evaluate the mechanism underlying the differential expression of mda-7 as a function of melanoma progression and induction of growth arrest and differentiation in human melanoma cells the promoter region of this gene has been isolated from a human placental genomic library and characterized. Sequence analysis by GCG identifies multiple recognition sites for the AP-1 and C/EBP transcription factors. Employing a heterologous mda-7 luciferase gene reporter system, we demonstrate that ectopic expression of either AP-1/cjun or C/EBP can significantly enhance expression of the mda-7 promoter in melanoma cells. In contrast, a dominant negative mutant of cJun, TAM67, is devoid of promoter-enhancing ability. Western blot analyses reveals that cJun and the C/EBP family member C/EBP-beta are physiologically relevant transcription factors

whose expression corresponds with mda-7 mRNA expression. Electrophoretic mobility shift assays (EMSA) performed using nuclear protein extracts from terminally differentiated human melanoma cells document binding to regions of the mda-7 promoter that correspond to consensus binding sites for AP-1 and C/EBP. These results provide further mechanistic insights into the regulation of the mda-7 gene during induction of terminal cell differentiation in human melanoma cells.

2/7/5
DIALOG(R)File 5:Biosis Previews(R)

0012458545 BIOSIS NO.: 200000176858
Regulation of mda-7 gene expression during human melanoma differentiation
AUTHOR: %%%Madireddi Malavi T%%%; Dent Paul; Fisher Paul B (Reprint
AUTHOR ADDRESS: Departments of Pathology and Urology, College of Physicians and Surgeons, Columbia University, New York, NY, 10032, USA**USA
JOURNAL: Oncogene 19 (10): p1362-1368 March 2, 2000 2000
MEDIUM: print
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Induction of irreversible growth arrest and terminal differentiation in human melanoma cells following treatment with recombinant human fibroblast interferon (IFN-beta) and mezerein (MEZ) results in elevated expression of a specific melanoma differentiation associated gene, mda-7. Experiments were conducted to define the mechanism involved in the regulation of mda-7 expression in differentiating human melanoma cells. The mda-7 gene is actively transcribed in uninduced HO-1 human melanoma cells and the rate of transcription of mda-7 is not significantly enhanced by treatment with IFN-beta, MEZ or IFN-beta + MEZ. The high basal activity of the mda-7 promoter in uninduced melanoma cells and the absence of enhancing effect upon treatment with differentiation inducers is corroborated by transfection studies using the promoter region of mda-7 linked to a luciferase reporter gene containing the SV40 polyadenylation signal sequence. RT-PCR analysis detects the presence of low levels of mda-7 transcripts in uninduced and concomitant increases in differentiation inducer treated HO-1 cells. However, steady-state mda-7 mRNA is detected only in IFN-beta + MEZ and to a lesser degree in MEZ treated cells. We show that induction of terminal differentiation of HO-1 cells with IFN-beta + MEZ dramatically increases the half-life of mda-7 mRNA while treatment with cycloheximide results in detectable mda-7 mRNA in control and inducer treated cells. These observations confirm constitutive activity of the mda-7 promoter in HO-1 cells irrespective of differentiation status suggesting posttranscriptional processes as important determinants of mda-7 expression during terminal differentiation. The 3' UTR region of mda-7 contains AU-rich elements (ARE) that contribute to rapid mda-7 mRNA turnover during proliferation and reversible differentiation, a process controlled by a labile protein factor(s). Substitution of the SV40 polyadenylation signal sequence in the luciferase reporter plasmid with the mda-7-ARE-3'-UTR renders the Luciferase message unstable when expressed in proliferating and reversibly differentiated melanoma cells. In contrast, the luciferase message is stabilized when the mda-7-ARE-3'-UTR construct is expressed in terminally differentiated HO-1 cells. These results provide compelling evidence that mda-7 expression during terminal differentiation in human melanoma cells is regulated predominantly at a posttranscriptional level.

2/7/6
DIALOG(R)File 5:Biosis Previews(R)

0011933351 BIOSIS NO.: 199900193011
Analysis of the mechanism of action of a novel melanoma differentiation associated gene with ubiquitous cancer growth suppressing properties, Mda-7, utilizing the tetracycline inducible system in HO-1 human melanoma

cells
AUTHOR: Gopalkrishnan R (Reprint); Christiansen K A; %%%Madireddi M T%%%; Su Z-Z; Fisher P B
AUTHOR ADDRESS: Dep. Pathol., Coll. Physicians Surgeons, Columbia Univ., New York, NY 10032, USA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 40 p734-735 March, 1999 1999
MEDIUM: print
CONFERENCE/MEETING: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999; 19990410
SPONSOR: American Association for Cancer Research
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/7
DIALOG(R)File 5:Biosis Previews(R)

0011748920 BIOSIS NO.: 199900008580
The cancer growth suppressor gene mda-7 selectively induces apoptosis in human breast cancer cells and inhibits tumor growth in nude mice
AUTHOR: Su Zao-Zhong; %%%Madireddi Malavi T%%%; Lin Jiao Jiao; Young Charles S H; Kitada Shinichi; Reed John C; Goldstein Neil I; Fisher Paul B (Reprint
AUTHOR ADDRESS: Dep. Urol., Columbia Univ., Coll. Physicians Surgeons, 630 W. 168th St., New York, NY 10032, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 95 (24): p14400-14405 Nov. 24, 1998 1998
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A differentiation induction subtraction hybridization strategy is being used to identify and clone genes involved in growth control and terminal differentiation in human cancer cells. This scheme identified melanoma differentiation associated gene-7 (mda-7), whose expression is upregulated as a consequence of terminal differentiation in human melanoma cells. Forced expression of mda-7 is growth inhibitory toward diverse human tumor cells. The present studies elucidate the mechanism by which mda-7 selectively suppresses the growth of human breast cancer cells and the consequence of ectopic expression of mda-7 on human breast tumor formation in vivo in nude mice. Infection of wild-type, mutant, and null p53 human breast cancer cells with a recombinant type 5 adenovirus expressing mda-7, Ad.mda-7 S, inhibited growth and induced programmed cell death (apoptosis). Induction of apoptosis correlated with an increase in BAX protein, an established inducer of programmed cell death, and an increase in the ratio of BAX to BCL-2, an established inhibitor of apoptosis. Infection of breast carcinoma cells with Ad.mda-7 S before injection into nude mice inhibited tumor development. In contrast, ectopic expression of mda-7 did not significantly alter cell cycle kinetics, growth rate, or survival in normal human mammary epithelial cells. These data suggest that mda-7 induces its selective anticancer properties in human breast carcinoma cells by promoting apoptosis that occurs independent of p53 status. On the basis of its selective anticancer inhibitory activity and its direct antitumor effects, mda-7 may represent a new class of cancer suppressor genes that could prove useful for the targeted therapy of human cancer.

2/7/8
DIALOG(R)File 5:Biosis Previews(R)

0011315291 BIOSIS NO.: 199800109538
Molecular determinants of growth control and terminal differentiation in

human melanoma cells
AUTHOR: %%%Madireddi Malavi T%%% (Reprint); Su Zao-Zhong; Lin Jiao Jiao (Reprint); Goldstein Neil I; Fisher Paul B (Reprint
AUTHOR ADDRESS: Herbert Irving Comprehensive Cancer Center., Columbia Univ., Coll. Physicians Surgeons, New York, NY 10032, USA**USA
JOURNAL: Anticancer Research 17 (5C): p3953-3954 Sept.-Oct., 1997 1997
MEDIUM: print
CONFERENCE/MEETING: Seventh International Conference on Differentiation Therapy Versailles, France October 5-8, 1997; 19971005
ISSN: 0250-7005
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/9
DIALOG(R)File 5:Biosis Previews(R)

0011313679 BIOSIS NO.: 199800107926
Inhibition of human cancer growth in nude mice using the novel tumor growth inhibitory gene mda-7
AUTHOR: Su Zao-Zhong (Reprint); %%%Madireddi Malavi T%%%; Lin Jiao Jiao; Young C S Hamish; Kitada Shunichii; Reed John C; Goldstein Neil I; Fisher Paul B
AUTHOR ADDRESS: Dep. Microbiol., Hebert Irving Comprehensive Cancer Cent., Coll. Physicians Surgeons Columbia Univ., New York, NY 10032, USA**USA
JOURNAL: Cancer Gene Therapy 4 (6 CONF. SUPPL.): pS14 Nov.-Dec., 1997 1997
MEDIUM: print
CONFERENCE/MEETING: Sixth International Conference on Gene Therapy of Cancer San Diego, California, USA November 20-22, 1997; 19971120
ISSN: 0929-1903
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/10
DIALOG(R)File 5:Biosis Previews(R)

0010916119 BIOSIS NO.: 199799550179
Programmed DNA degradation and nucleolar biogenesis in occur in distinct organelles during macronuclear development in Tetrahymena
AUTHOR: Smothers James F; %%%Madireddi Malavi T%%%; Warner Fred D; Allis C David (Reprint
AUTHOR ADDRESS: Dep. Biol., Univ. Rochester, Rochester, NY 14627, USA**USA
JOURNAL: Journal of Eukaryotic Microbiology 44 (2): p79-88 1997 1997
ISSN: 1066-5234
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Programmed DNA rearrangements, including DNA degradation, characterize the development of the soma from the germline in a number of developmental systems. Pdd1p (programmed DNA degradation 1 protein), a development-specific polypeptide in Tetrahymena, is enriched in developing macronuclei (anlagen) and has been implicated in DNA elimination and nucleolar biogenesis. Here, immunocytochemistry and fluorescent in situ hybridization (FISH) were employed to follow Pdd1p and two nucleolar markers (Nopp52 and rDNA) during macronuclear development. Both Pdd1p and Nopp52 localize to subnuclear structures, each of which resemble nucleoli. However, while true nucleoli form and persist during development, Pdd1p-positive structures are only present for a brief period of macronuclear differentiation. Accordingly, two distinct organelles can be recognized in anlagen: (1) Pdd1p-positive structures, which lack Nopp52 and rDNA, and (2) developing nucleoli which contain rDNA and Nopp52 but lack Pdd1p. Taken together with recent data corroborating Pdd1p's role in DNA elimination, we favor the hypothesis that Pdd1p structures are unique, short-lived organelles, likely to function in programmed DNA degradation and not in nucleolar biogenesis.

2/7/11
DIALOG(R)File 5:Biosis Previews(R)

0010770925 BIOSIS NO.: 199799404985
An abundant nucleolar phosphoprotein is associated with ribosomal DNA in Tetrahymena macronuclei
AUTHOR: McGrath Kathleen E; Smothers James F; Dadd Christopher A; %%%Madireddi Malavi T%%%; Gorovsky Martin A; Allis C David (Reprint
AUTHOR ADDRESS: Dep. Biol., Univ. Rochester, Rochester, NY 14627, USA**USA
JOURNAL: Molecular Biology of the Cell 8 (1): p97-108 1997 1997
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An abundant 52-kDa phosphoprotein was identified and characterized from macronuclei of the ciliated protozoan Tetrahymena thermophila. Immunoblot analyses combined with light and electron microscopic immunocytochemistry demonstrate that this polypeptide, termed Nopp52, is enriched in the nucleoli of transcriptionally active macronuclei and missing altogether from transcriptionally inert micronuclei. The cDNA sequence encoding Nopp52 predicts a polypeptide whose amino-terminal half consists of multiple acidic/serine-rich regions alternating with basic/proline-rich regions. Multiple serines located in these acidic stretches lie within casein kinase II consensus motifs, and Nopp52 is an excellent substrate for casein kinase II in vitro. The carboxyl-terminal half of Nopp52 contains two RNA recognition motifs and an extreme carboxyl-terminal domain rich in glycine, arginine, and phenylalanine, motifs common in many RNA processing proteins. A similar combination and order of motifs is found in vertebrate nucleolin and yeast NSR1, suggesting that Nopp52 is a member of a family of related nucleolar proteins. NSR1 and nucleolin have been implicated in transcriptional regulation of rDNA and rRNA processing. Consistent with a role in ribosomal gene metabolism, rDNA and Nopp52 colocalize in situ, as well as by cross-linking and immunoprecipitation experiments, demonstrating an association between Nopp52 and rDNA in vivo.

2/7/12
DIALOG(R)File 5:Biosis Previews(R)

0010612519 BIOSIS NO.: 199699246579
Pdd1p, a novel chromodomain-containing protein, links heterochromatin assembly and DNA elimination in tetrahymena
AUTHOR: %%%Madireddi Malavi T%%% (Reprint); Coyne Robert S; Smothers James F (Reprint); Mickey Katherine M; Yao Meng-Chao; Allis C David (Reprint
AUTHOR ADDRESS: Columbia Presbyterian Cancer Cent., New York, NY 07024, USA **USA
JOURNAL: Cell 87 (1): p75-84 1996 1996
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: During Tetrahymena conjugation, programmed DNA degradation occurs in two separate nuclei. Thousands of germline-specific deletion elements are removed from the genome of the developing somatic macronucleus, and the old parental macronucleus is degraded by an apoptotic mechanism. An abundant polypeptide, Pdd1p (formerly p65), localizes to both of these nuclei at the time of DNA degradation. Here we report that, in developing macronuclei, Pdd1p localizes to electron-dense, heterochromatic structures that contain germline-specific deletion elements. Pdd1p also associates with parental macronuclei during terminal stages of apoptosis. Sequencing of the PDD1 gene reveals it to be a member of the chromodomain family, suggesting a molecular link between heterochromatin assembly and programmed DNA degradation.

2/7/13
DIALOG(R)File 5:Biosis Previews(R)

0010059466 BIOSIS NO.: 199598527299
Waste not, want not: Does DNA elimination fuel gene amplification during development in ciliates?
AUTHOR: %%%Madireddi Malavi T%%% (Reprint); Smothers James F (Reprint); Allis C David
AUTHOR ADDRESS: Dep. Biol., Syracuse Univ., Syracuse, NY 13244, USA**USA
JOURNAL: Seminars in Developmental Biology 6 (5): p305-315 1995 1995
ISSN: 1044-5781
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Citation
LANGUAGE: English

2/7/14
DIALOG(R)File 5:Biosis Previews(R)

0009538624 BIOSIS NO.: 199598006457
Identification of a Novel Polypeptide Involved in the Formation of DNA-Containing Vesicles during Macronuclear Development in Tetrahymena
AUTHOR: %%%Madireddi Malavi T%%%; Davis Maria C; Allis C David (Reprint
AUTHOR ADDRESS: Dep. Biol., Syracuse Univ., Syracuse, NY 13244, USA**USA
JOURNAL: Developmental Biology 165 (2): p418-431 1994 1994
ISSN: 0012-1606
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An abundant phosphoprotein with an apparent molecular mass of 65 kDa (p65) has been identified that is enriched in developing new macronuclei (or anlagen) isolated from the holotrichous ciliate, Tetrahymena thermophila. During early stages of macronuclear development, p65 is actively synthesized and deposited into young (4C) anlagen and is not found in micronuclei or parental macronuclei. p65 is not detected in older (8C) anlagen or in vegetatively growing or starved cells, and thus p65 is under stringent developmental control. In situ analyses, using polyclonal antibodies generated against p65, demonstrate that p65 undergoes a pronounced change in distribution during anlagen differentiation. Initially, anlagen are uniformly stained with these antibodies. However, following separation of conjugants, this staining pattern converts to one that is punctate and fragmented. As development proceeds, most, if not all, of these p65-based particles become peripherally located in anlagen and appear as well-defined vesicles surrounding a discrete central core of DNA of yet undetermined origin. This remarkable cytological distribution suggests an involvement of p65 in the elimination or processing of DNA during anlagen differentiation. If the above is correct, p65 provides the first inroad into the protein machinery involved in the well-known DNA rearrangements that characterize ciliate macronuclear development.
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